

### **REMARKS**

Claims 1-53 are currently pending and presented for examination. Applicants have made clarifying amendments to dependent claims 33, 38 and 51 and have added dependent claims 54-56. Applicants respectfully request that the Examiner enter each of the amendments and new claims because none of the amendments or new claims raise new issues.

Support for these new dependent claims can be found throughout the specification and claims as originally filed. For example, support for each of dependent claims 54-56 can be found at paragraphs [0030], [0036], [0041], [0064], [0081]-[0084] and elsewhere throughout the specification as originally filed.

Claims 33, 38, and 51 are amended to recite, in relevant part, "the change in difference." Support for these amendments can be found throughout the specification and claims as originally filed. For example, support for each of these amendments can be found at paragraph [0090], Figure 5 and elsewhere throughout the specification as originally filed.

In addition to the foregoing, Applicants respectfully submit that none of the amendments or new claims raise new issues, and thus, each can be entered subsequent to a final Office Action. In particular, the amendment to each of the dependent claims is simply for clarification. Additionally, the subject matter of the three new dependent claims falls within the scope of the subject matter already searched in connection with independent claims 1, 9 and 39. Accordingly, applicants request that the Examiner enter each of the amendments and new claims.

Applicant would like to thank the Examiners for the helpful discussion during the personal interview on November 9, 2010. In view of this discussion, Applicants present the following remarks.

#### **35 U.S.C. § 112, first paragraph**

Claims 30-31, 35-36, 48-49 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to be adequately supported by the specification as originally filed. In particular, the Examiner asserts that although the specification discloses a program that decides whether to continue synthesis based on one or more criteria, the specification allegedly does not describe a program that resumes delivery to wells where failure was previously indicated.

Applicants respectfully submit that the specification provides explicit support for embodiments that include resuming delivery to wells where failure was previously indicated. For example, as agreed during the interview of November 9, 2010, among other things, paragraph [0076] describes embodiments that include automatically stopping and restarting synthesis. For at least the foregoing reason, Applicants respectfully submit that the specification as filed fully supports the subject matter recited in the above-rejected dependent claims. Accordingly, Applicants request that the rejection of Claims 30-31, 35-36, 48-49 under 35 U.S.C. § 112, first paragraph be withdrawn.

### **35 U.S.C. § 112, second paragraph**

Claims 33, 38, and 51 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being unclear. In particular, the Examiner alleges that the phrase “increasingly negative slope” should be characterized as a change in difference between the value expected and the specific value over a period of time.

To expedite prosecution of the instant application, Claims 33, 38 and 51 are amended, as the Examiner suggests, to recite, in relevant part, “the change in difference between the value expected if the chemical reaction is successful and said specific value.” Accordingly, Applicant respectfully requests that the rejection of Claims 33, 38, and 51 under 35 U.S.C. § 112, second paragraph be withdrawn.

### **RESPONSE TO OBVIOUSNESS REJECTIONS**

In addition to the new arguments provided below, in connection with each of the obviousness rejections set forth in the instant Office Action, Applicants reiterate and maintain each of their arguments from each of their previously-filed responses.

### **35 U.S.C. § 103(a) – The combination of Balch and VanBrunt et al.**

#### Rejection of claims 1-3, 6-10, 13-16, 18-19, 29, 32, 34, 37, 39-43, 46, 47 and 52-53

The Examiner rejects claims 1-3, 6-10, 13-16, 18-19, 29, 32, 34, 37, 39-43, 46, 47 and 52-53 under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,083,763 (Balch) in

view of U.S. Patent Application Publication No. 2004/0067164 (VanBrunt et al.). In particular, the Examiner asserts that Balch discloses all of the elements of the above-rejected claims other than an aspiration means and “a dispenser that is configured to discontinue dispensing of reagents to wells where a reaction is not taking place” (see Office Action at pages 3-4). The Examiner, however, asserts that this deficiency is remedied by VanBrunt et al., who allegedly disclose an apparatus having an aspiration means that is configured to abort further processing in vessels where the detector does not detect a reaction. The Examiner then contends that a skilled artisan would have combined the dispenser configuration disclosed by VanBrunt et al. with the instrument allegedly disclosed by Balch in order to “save time and cost” (see Office Action at page 5).

Applicants maintain that claims 1-3, 6-10, 13-16, 18-19, 29, 32, 34, 37, 39-43, 46, 47 and 52-53 are not obvious over the combination of Balch and VanBrunt et al because the modified system fails to teach or suggest all of the elements of any of the above-rejected independent claims. In addition, a skilled artisan would not be motivated to modify the system of Balch as described by the Examiner to arrive at the subject matter recited in the independent claims.

Regarding the combination of Balch and VanBrunt et al., the Examiner asserts that Balch discloses an automated molecular analyzer at Figures 1 and 9. The Examiner further asserts that the analyzer comprises each of the remaining elements of the above-rejected independent claims other than a dispenser configured for dispensing reagents where a reaction is not taking place and an aspiration means. *See Office Action, pages 3-4.* The Examiner asserts, however, that a skilled artisan would modify the instruments disclosed by Balch so that the dispenser stops delivering reagents to wells that are not exhibiting any reactions in order to save time and cost. *See Office Action, page 5.* Applicants respectfully disagree.

Applicants submit that the combination of Balch and VanBrunt et al. does not teach or suggest all of the elements of any of the independent claims. Specifically, Applicants submit that Balch discloses a dispenser system for making an array (see Figure 4, column 7, lines 9-10) and a separate analyzer system for detecting molecules that hybridize to the probes attached to the array (see Figure 1, column 7, lines 2-3). It is clear from columns 9-16, Figure 4 and elsewhere throughout the Balch reference that the dispenser is an array of capillary tubes used to attach probe molecules to the surface of a substrate thereby forming an array of probe molecules. Balch

does not further discuss the dispenser system other than in connection with the construction of the array. Furthermore, Balch does not in anyway teach or suggest detecting the coupling reaction that occurs when coupling the probes to the surface of the substrate in order to make the array. Rather, Balch discloses using the arrays to detect hybridization events between an array probe and a complementary molecule using the analyzer system of Figure 1. As such, the analyzer system does not detect the extent of the chemical reaction for which the dispenser system is employed (that is, for coupling the probe to the substrate). Rather, the analyzer system detects only hybridization of sample molecules with array probes. However, detecting whether a hybridization event occurs when the array is contacted with a sample is not a measure of the extent of the coupling reactions during array synthesis. Thus, even if it is assumed, *arguendo*, that a skilled artisan would adapt the system of Balch, with the analyzer program disclosed by VanBrunt et al., the modified analyzer system of Balch would monitor hybridization events but not the chemical coupling reaction where the dispenser system of Balch is utilized. As such, the combination of Balch and VanBrunt et al. does not teach the use of an analyzer program for determining a specific value corresponding to the extent of chemical reaction within each well in order to configure a dispenser to maintain delivery of reagents depending on extent of that chemical reaction as recited in the independent claims.

In addition to the foregoing, Applicants submit that a skilled artisan would not be motivated to modify the systems of Balch in accordance with the disclosure of VanBrunt et al. so as to incorporate an analyzer program that monitors the extent of chemical reactions in order to stop dispensation of reagents to wells where reaction failure is indicated while maintaining delivery to wells where failure is not indicated. Irrespective of whether the dispenser and analyzer systems disclosed by Balch function separately or together, a skilled artisan would not be motivated to make the above-described modification because there are no subsequent dispensation steps in the array synthesis. Because coupling the probe to the surface of the substrate is performed in one step, no further dispensation to the substrate occurs subsequent to the initial probe placement. As such, further dispensation of reagents for the reaction would not be necessary regardless of whether or not the coupling reaction were successful. Accordingly, a skilled artisan would have absolutely no motivation to adapt the systems disclosed by Balch in

accordance with the disclosure of VanBrunt et al. to arrive at the subject matter recited in any of the above-rejected independent claims.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the above rejection of claims 1-3, 6-10, 13-16, 18-19, 29, 32, 34, 37, 39-43, 46, 47 and 52-53.

Rejection of claims 4, 5 and 17

The Examiner rejects claims 4, 5 and 17 under 35 U.S.C. § 103(a) as allegedly obvious over Balch in view of VanBrunt et al. and further in view of U.S. Patent No. 6,448,064 (Vo Dinh et al.). The Examiner acknowledges that neither Balch nor VanBrunt et al. disclose the use of LEDs to excite the sample. The Examiner, however, asserts that this missing element is disclosed by Vo Dinh et al. The Examiner then contends that a skilled artisan would have combined the disclosures of Balch, VanBrunt et al. and Vo Dinh et al. to arrive at the subject matter recited in claims 4, 5 and 17 since LEDs are cheaper than lasers. Furthermore, the Examiner asserts that the skilled artisan would have used a plurality of LEDs since such an arrangement would allegedly increase efficiency.

Applicants submit that claims 4, 5 and 17 are not obvious under 35 U.S.C. § 103(a). As discussed above, the combination of Balch and VanBrunt et al. also does not teach or suggest the arrangement of the elements as set forth in the above-rejected independent claims from which claims 4, 5 and 17 depend. Vo Dinh et al. do not remedy this deficiency. As further discussed above, a skilled artisan would not combine the disclosure of Balch with that of VanBrunt et al. Vo Dinh et al. do not remedy this deficiency. As such, none of claims 4, 5 or 17 are obvious over any of the above-recited combinations of references.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of claims 4, 5 and 17 under 35 U.S.C. § 103(a).

Rejection of claims 11 and 12

The Examiner rejects claims 11 and 12 under 35 U.S.C. § 103(a) as allegedly obvious over Balch in view of VanBrunt et al. and further in view of U.S. Patent Application Publication No. 2003/0207441 (Eyster et al.) (claim 11) or Balch in view of VanBrunt et al. and further in

view of U.S. Patent No. 5,639,603 (Dower et al.) (claim 12). The Examiner acknowledges that neither Balch nor VanBrunt et al. disclose a computer configured to generate a warning message as recited in claim 11 or a liquid removal device comprising a centrifuge as recited in claim 12. The Examiner, however, asserts that these missing elements are disclosed by Eyster et al. and Dower et al., respectively. The Examiner then contends that a skilled artisan would have combined the disclosures of Balch, VanBrunt et al. and Eyster et al. to arrive at the subject matter recited in claim 11 and the disclosures of Balch, VanBrunt et al. and Dower et al. to arrive at the subject matter recited in claim 12.

Applicants submit that claims 11 and 12 are not obvious under 35 U.S.C. § 103(a). As discussed above, the combination of Balch and VanBrunt et al. does not teach or suggest the arrangement of the elements as set forth in independent claim 9, from which claims 11 and 12 depend. Neither Eyster et al. nor Dower et al. remedy this deficiency. As further discussed above, a skilled artisan would not combine the disclosure of Balch with that of VanBrunt et al. Neither Eyster et al. nor Dower et al. remedy this deficiency. As such, neither claim 11 nor 12 are obvious over any of the above-recited combinations of references.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of claims 11 and 12 under 35 U.S.C. § 103(a).

**35 U.S.C. § 103(a) – The combination of Balch and Hartwich et al.**

Rejection of claims 1-19, 29, 32, 34, 37, 39-43, 46, 47, 52 and 53

The Examiner rejects claims 1-4, 6-8, 29, 32, 39-43, 46, 47, 52 and 53 as allegedly obvious under 35 U.S.C. § 103(a) over Balch in view of PCT Application Publication No. WO01/69210 (Hartwich et al.). In particular, the Examiner asserts that Balch discloses all of the elements of the above-rejected claims other than “a dispenser that is configured to discontinue dispensing of reagents to wells where a reaction is not taking place.” *Office Action, page 7*. The Examiner, however, asserts that in view of the disclosure of Hartwich et al., a skilled artisan would have configured the dispenser allegedly disclosed by Balch as specified in the above-rejected claims in order to “save time and cost.” *Office Action, page 8*. In addition to the foregoing rejection, the Examiner rejects claim 5 as allegedly obvious over the combination of

Balch and Hartwich et al. in view of Vo Dinh et al. The Examiner also rejects claims 9, 10, 13-16, 18, 19, 34 and 37 as allegedly obvious over the combination of Balch and Hartwich et al. in view of U.S. Patent No. 6,485,913 (Becker et al.) and claim 11 as allegedly obvious over the combination of Balch, Hartwich et al. and Becker et al. in view of Eyster et al. Additionally, the Examiner rejects claim 12 as allegedly obvious over the combination of Balch and Hartwich et al. and Becker et al. in view of Dower et al., and finally, the Examiner rejects claim 17 as allegedly obvious over the combination of Balch, Hartwich et al. and Becker et al. in view of Vo Dinh et al.

Applicants maintain that none of the above-rejected claims are obvious over any combination of the above-cited references. As discussed in connection with the combination of Balch and VanBrunt et al., the combination of Balch and Hartwich et al. does not teach or suggest all of the elements of any of the above-rejected claims. Specifically, as discussed above, Balch discloses a dispenser system for making an array and an analyzer system for detecting hybridization of molecules to the array. Modifying the analyzer system of Balch in view of the disclosure of Hartwich does not result in the claimed subject matter because the hybridization events being monitored are neither connected to the making of the array nor do they require maintaining reagent dispensation for furtherance of the hybridizations. As such, continued dispensation of reagents would not occur regardless of whether the analyzer is modified to monitor success or failure of the hybridization events.

In addition to the foregoing, a skilled artisan would not be motivated to modify the system of Balch as described by the Examiner to arrive at the subject matter recited in the above-rejected claims. As discussed above, irrespective of whether the dispenser and analyzer systems disclosed by Balch function separately or together, a skilled artisan would not be motivated to make the above-described modification because there are no subsequent dispensation steps in the array synthesis. Because coupling the probe to the surface of the substrate is performed in one step, no further dispensation to the substrate occurs subsequent to the initial probe placement. As such, further dispensation of reagents for the reaction would not be necessary regardless of whether or not the coupling reaction were successful. Accordingly, a skilled artisan would have absolutely no motivation to adapt the systems disclosed by Balch in accordance with the

disclosure of Hartwich et al. to arrive at the subject matter recited in any of the above-rejected claims.

In view of the foregoing remarks, Applicants submit that none of claims 1-19, 29, 32, 34, 37, 39-43, 46, 47, 52 and 53 are obvious. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection of claims 1-19, 29, 32, 34, 37, 39-43, 46, 47, 52 and 53 under 35 U.S.C. § 103(a).

**35 U.S.C. § 103(a) – The combination of Balch and Davies et al.**

Rejection of claims 39-47, 50, 52 and 53

The Examiner rejects claims 39-47, 50, 52 and 53 as allegedly obvious under 35 U.S.C. § 103(a) over Balch in view of United States Patent Application Publication No. US2003/0143591 (Davies et al.). In particular, the Examiner asserts that Balch discloses all of the elements of the above-rejected claims other than “a dispenser that is configured to discontinue dispensing of reagents to wells where a reaction is not taking place.” *Office Action, page 12*. The Examiner, however, asserts that in view of the disclosure of Davies et al., a skilled artisan would “provide the analyzer disclosed by Balch with a program that monitors the progress of PCR reactions in real time based on DMT concentration and ceases processing of test sites exhibiting failed or inefficient reactions.” *Office Action, page 13*.

Applicants maintain that none of the above-rejected claims are obvious over the combination of Balch and Davies. As discussed in connection with the other combinations of references, the combination of Balch and Davies et al. does not teach or suggest all of the elements of any of the above-rejected claims. Specifically, as discussed above, Balch discloses a dispenser system for making an array and an analyzer system for detecting hybridization of molecules to the array. Modifying the analyzer system of Balch in view of the disclosure of Davies does not result in the claimed subject matter because the hybridization events being monitored are neither connected to the making of the array nor do they require maintaining reagent dispensation for furtherance of the hybridizations. As such, continued dispensation of reagents would not occur regardless of whether the analyzer is modified to monitor success or failure of the hybridization events.



In addition to the foregoing, a skilled artisan would not be motivated to modify the system of Balch as described by the Examiner to arrive at the subject matter recited in the above-rejected claims. As discussed above, irrespective of whether the dispenser and analyzer systems disclosed by Balch function separately or together, a skilled artisan would not be motivated to make the above-described modification because there are no subsequent dispensation steps to control in the array synthesis. Because coupling the probe to the surface of the substrate is performed in one step, no further dispensation to the substrate occurs subsequent to the initial probe placement. As such, further dispensation of reagents for the reaction would not be necessary regardless of whether or not the coupling reaction were successful. Accordingly, a skilled artisan would have absolutely no motivation to adapt the systems disclosed by Balch in accordance with the disclosure of Hartwich et al. to arrive at the subject matter recited in any of the above-rejected claims.

In view of the foregoing remarks, Applicants submit that none of claims 39-47, 50, 52 and 53 are obvious. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection of claims 39-47, 50, 52 and 53 under 35 U.S.C. § 103(a).

**No Disclaimers or Disavowals**

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

**Application No.:** 10/762,931  
**Filing Date:** January 21, 2004

### **CONCLUSION**

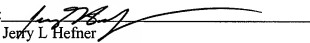
Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

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